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# FACSIMILE MESSAGE

TO:

Examiner Srivastava

FACSIMILE #:

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FROM:

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RF:

Draft Claims for 10/660,093

DATE:

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CALL (405) 607-8600, SHOULD YOU HAVE ANY QUESTIONS REGARDING THIS TRANSMITTAL. \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*

#### Examiner.

Thank you for reviewing these draft claims. I look forward to discussing them with you at your convenience.

Best Regards,

Douglas J. Sorocco

## PROPOSED CLAIM AMENDMENTS IN US SERIAL NO. 10/660,093 IN **RESPONSE TO DECEMBER 28, 2007 OFFICE ACTION**

1. (Previously Presented) A method for alleviating chronic pain in a subject, the method comprising the steps of:

administering an effective amount of at least one inhibitor of neurotransmitter synthesis to a subject suffering from chronic pain at a peripheral nervous system inflammation site, wherein the at least one inhibitor of neurotransmitter synthesis is selected from the group consisting of a glutamine synthetase inhibitor, a glutamate dehydrogenase inhibitor, a pyruvate carboxylase inhibitor, a glutamine cycle inhibitor, a glial cell tricarboxylic acid cycle inhibitor, and combinations thereof: and

wherein the administration of the effective amount of at least one inhibitor of neurotransmitter synthesis results in inhibition in synthesis of at least one neurotransmitter in the peripheral nervous system of the subject at the peripheral nervous system inflammation site, thereby resulting in a reduction in glutamate stimulation of peripheral sensory nerve fibers, whereby a reduction in nociceptive responses at the peripheral nervous system inflammation site is observed without any resulting acute pain behavior.

## 2-3. (Canceled)

- (Previously Presented) The method of claim 1, wherein the subject is a human.
- 5. (Previously Presented) The method of claim 1, wherein the step of administering an effective amount of at least one inhibitor of neurotransmitter synthesis to a subject suffering from chronic pain at a peripheral nervous system inflammation site is further defined as locally administering an effective amount of at least one inhibitor of neurotransmitter synthesis to a subject suffering from chronic pain at a peripheral nervous system inflammation site.
- 6. (Previously Presented) The method of claim 1, wherein the step of administering an effective amount of at least one inhibitor of neurotransmitter synthesis to a subject suffering from chronic pain at a peripheral nervous system inflammation site is further defined as injecting an effective amount of at least one inhibitor of neurotransmitter synthesis to a subject suffering from chronic pain at a peripheral nervous system inflammation site.
- (Previously Presented) The method of claim 1, wherein the step of administering an effective amount of at least one inhibitor of neurotransmitter

synthesis to a subject suffering from chronic pain at a peripheral nervous system inflammation site is further defined as topically applying an effective amount of at least one inhibitor of neurotransmitter synthesis to a subject suffering from chronic pain at a peripheral nervous system inflammation site.

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- 8. (Previously Presented) The method of claim 1, wherein the step of administering an effective amount of at least one inhibitor of neurotransmitter synthesis to a subject suffering from chronic pain at a peripheral nervous system inflammation site is further defined as orally administering an effective amount of at least one inhibitor of neurotransmitter synthesis to a subject suffering from chronic pain at a peripheral nervous system inflammation site.
- (Previously Presented) The method of claim 8, wherein the effective 9. amount of at least one inhibitor of neurotransmitter synthesis is in the form of a prodrug.
- 10. (Previously Presented) The method of claim 8, wherein the effective amount of at least one inhibitor of neurotransmitter synthesis demonstrates substantially no penetration across the central nervous system blood brain harrier.

11. (Previously Presented) The method of claim 1, wherein the administration of the effective amount of at least one inhibitor of neurotransmitter synthesis results in a reduction in nociceptive responses at the peripheral nervous system inflammation site for at least two days without any resulting acute pain behavior.

### 12-18. (Canceled)

- 19. (Previously Presented) A method for alleviating acute and chronic pain in a subject, the method comprising the steps of:
  - administering an effective amount of at least one inhibitor of neurotransmitter synthesis to a subject suffering from acute and chronic pain at a peripheral nervous system inflammation site, wherein the at least one inhibitor of neurotransmitter synthesis is selected from the group consisting of a glutamine synthetase inhibitor, a glutamate dehydrogenase inhibitor, a pyruvate carboxylase inhibitor, a glutamine cycle inhibitor, a glial cell tricarboxylic acid cycle inhibitor, and combinations thereof:
  - administering an effective amount of at least one compound having analgesic effects to the subject at the peripheral nervous system inflammation site: and

wherein the administration of the effective amount of at least one inhibitor of neurotransmitter synthesis results in inhibition of at least one neurotransmitter in the peripheral nervous system of the subject at the peripheral nervous system inflammation site, thereby resulting in a reduction in glutamate stimulation of peripheral sensory nerve fibers, and the administration of the effective amount of at least one compound having analgesic effects results in a decrease in nociceptive responses at the peripheral nervous system inflammation site without any resulting acute pain behavior.

#### 20-21. (Canceled)

- 22. (Original) The method of claim 19 wherein, in the step of administering an effective amount of at least one compound having analysesic effects, the at least one compound having analysesic effects is a glutamate antagonist or an inhibitor of glutamate binding to glutamate receptors on peripheral sensory nerves.
- 23. (Previously Presented) The method of claim 19, wherein the administration of the effective amount of at least one inhibitor of neurotransmitter synthesis and the administration of the effective amount of at

least one compound having analgesic effects results in a decrease in nociceptive responses at the peripheral nervous system inflammation site that last for a period of at least two days without any resulting acute pain behavior.

- 24. (Newly Added) The method of claim 1 wherein, in the step of administering an effective amount of at least one inhibitor of neurotransmitter synthesis, the at least one inhibitor of neurotransmitter synthesis is a glutamine synthetase inhibitor selected from the group consisting of methionine-S-sulfoximine (MSO), phosphinothricin (PPT), 4-N-hydroxy-L-2,4-diaminobutyric acid (NH-DABA), Delta-hydroxylysine, and combinations thereof.
- 25. (Newly Added)The method of claim 1 wherein, in the step of administering an effective amount of at least one inhibitor of neurotransmitter synthesis, the at least one inhibitor of neurotransmitter synthesis is a glutamate dehydrogenase inhibitor selected from the group consisting of bromofuroate, Palmitoyl-Coenzyme-A (Palmitoyl-Co-A), orthovanadate, vanadyl sulphate, vanadyl acetylacetonate, glutarate, 2-oxoglutarate (a-ketoglutarate), estrogen, estrogen analogues, pyridine-2,6-dicarboxylic acid, and combinations thereof.
- 26. (Newly Added) The method of claim 1 wherein, in the step of administering an effective amount of at least one inhibitor of neurotransmitter

synthesis, the at least one inhibitor of neurotransmitter synthesis is a pyruvate carboxylase inhibitor selected from the group consisting of phenyl acetic acid (PAA), phenylacetyl Coenzyme-A, phenylacetyl Co-A ester, oxamate, and combinations thereof.

- 27. (Newly Added) The method of claim 1 wherein, in the step of administering an effective amount of at least one inhibitor of neurotransmitter synthesis, the at least one inhibitor of neurotransmitter synthesis is a glial cell tricarboxylic acid cycle inhibitor selected from the group consisting of fluoroacetate, fluorocitrate, and combinations thereof.
- 28. (Newly Added) The method of claim 19 wherein, in the step of administering an effective amount of at least one inhibitor of neurotransmitter synthesis, the at least one inhibitor of neurotransmitter synthesis is a glutamine synthetase inhibitor selected from the group consisting of methionine-S-sulfoximine (MSO), phosphinothricin (PPT), 4-N-hydroxy-L-2,4-diaminobutyric acid (NH-DABA), Delta-hydroxylysine, and combinations thereof.
- 29. (Newly Added)The method of claim 19 wherein, in the step of administering an effective amount of at least one inhibitor of neurotransmitter synthesis, the at least one inhibitor of neurotransmitter synthesis is a glutamate

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- 30. (Newly Added) The method of claim 19 wherein, in the step of administering an effective amount of at least one inhibitor of neurotransmitter synthesis, the at least one inhibitor of neurotransmitter synthesis is a pyruvate carboxylase inhibitor selected from the group consisting of phenyl acetic acid (PAA), phenylacetyl Coenzyme-A, phenylacetyl Co-A ester, oxamate, and combinations thereof.
- 31. (Newly Added) The method of claim 19 wherein, in the step of administering an effective amount of at least one inhibitor of neurotransmitter synthesis, the at least one inhibitor of neurotransmitter synthesis is a glial cell tricarboxylic acid cycle inhibitor selected from the group consisting of fluoroacetate, fluorocitrate, and combinations thereof.